

CLAIMS

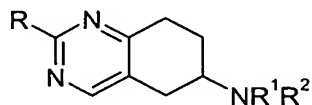
1. A composition comprising (I) a dopamine D2-receptor agonist, and (II) an anti-cholinergic agent comprising a member selected from the group consisting of tiotropium and pharmaceutically acceptable salts, anions, isomers, isotopes, polymorphs, hydrates and solvates thereof, in an effective therapeutic amount to treat inflammatory disease or obstructive airways disease.

2. The composition according to Claim 1 wherein the obstructive airways disease is asthma, COPD, or other obstructive airways disease exacerbated by bronchial hyper-reactivity and bronchospasm.

3. The composition according to Claim 1 wherein the dopamine D2-receptor agonist is a member selected from the group consisting of:

(a) alentemol; apomorphine; biperiden; bromocriptine; cabergoline; carboxirole; ciladopa; dopexamine; fenoldopam; ibopamine; levodopa; lisuride; methylenedioxypromethamphetamine; naxagolide; *N*-allylnoraporphine; pergolide; pramipexole; propylnorapomorphine; protokylol; quinagolide; quinpirole; ropinirole; roxindole; talipexole; terguride; trihexyphenidyl; and trihydroxyaporphine; and salts and combinations thereof;

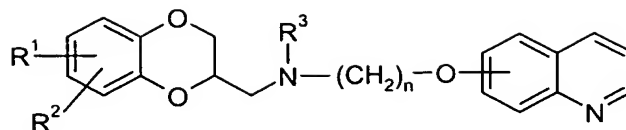
(b) a compound of Formula (0.0.1):



(0.0.1)

wherein R is -H, -OH, (C₁-C₄) alkylcarbonyloxy-, (C₁-C₄) alkylthio-, or -NR^aR^b where R^a and R^b are independently -H, -CH₃, -CH₂CH₃, or *n*-propyl; and R¹ and R² are independently -CH₃, -CH₂CH₃, *n*-propyl, or allyl; or a pharmaceutically acceptable salt thereof;

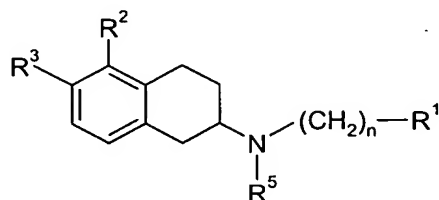
(c) a compound of Formula (0.0.2):



(0.0.2)

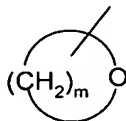
wherein n is 2-4; R^1 and R^2 are independently $-H$, $-(C_1-C_6)$ alkyl, $-(C_1-C_6)$ alkoxy, $-(C_7-C_{12})$ arylalkoxy, $-(C_2-C_6)$ alkanoyloxy, $-OH$, halo, $-NH_2$, mono- or di- $-(C_1-C_6)$ alkylamino; $-(C_2-C_6)$ alkanamido; or sulfonamido; R^3 is $-H$, or $-(C_1-C_6)$ alkyl; or R^1R^2 together are methylenedioxy, ethylenedioxy, or propylenedioxy; or a pharmaceutically acceptable salt thereof;

(d) a compound of Formula (0.0.3):



(0.0.3)

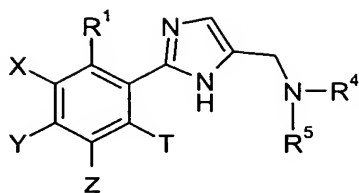
wherein R^2 is OA; and R^3 is $-H$ or OA; where A is $-H$, a hydrocarbyl radical of 1 to 3 carbon atoms, $-C(=O)R^4$, $-C(=O)NHR^4$, $-C(=O)N(R^4)_2$, or $-C(=O)OR^4$; provided that when R^2 and R^3 are OA, then R^2 and R^3 may be bonded together to form $-O-CH_2-O-$, or $-O-C(=O)-O-$; R^4 is (C_1-C_6) alkyl or an aromatic residue of 1-20 carbon atoms; n is 1-4; R^5 is unbranched (C_1-C_3) alkyl, or cyclopropylmethyl; and R^1 is (C_1-C_3) alkoxy, (C_3-C_6) cycloalkoxy, or a cyclic ether of partial Formula (0.1.1):



(0.1.1)

where m is 3 to 5; provided that when R^1 is (C_1-C_3) alkoxy, then R^3 cannot be $-H$; or a pharmaceutically acceptable salt thereof;

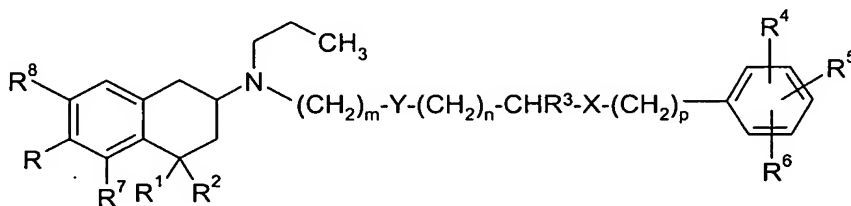
(e) a compound of Formula (0.0.4):



(0.0.4)

wherein R^1 and T are -H; halo; -OH; straight or branched (C_1 - C_6) alkyl; or straight or branched (C_1 - C_6) alkoxy; X and Z have the same meaning as R^1 and T additionally including SO_2R^6 where R^6 is straight or branched (C_1 - C_6) alkyl; Y is -H; halo; - NH_2 ; or straight or branched (C_1 - C_6) alkyl; R^4 and R^5 are -H; straight or branched (C_1 - C_6) alkyl; phenyl(C_1 - C_6)alkyl; or pyridyl(C_1 - C_6)alkyl; and $-NR^4R^5$ is 2-(1,2,3,4-tetrahydroisoquinolinyl) substituted by 0 to 2 of halo; -OH; straight or branched (C_1 - C_6) alkyl; or straight or branched (C_1 - C_6) alkoxy; or a pharmaceutically acceptable salt thereof;

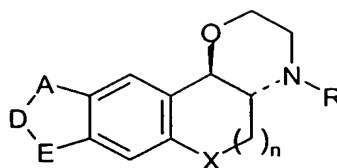
(f) a compound of Formula (0.0.5):



(0.0.5)

wherein m is 4 to 8; R, R^7 , and R^8 are H or OH, provided at least one is H but not all three are H and provided R^7 and R^8 are not both OH, or one of R^7 and R^8 is H and the other is $NHCHO$, $NHCH_3$, $NHSO_2CH_3$, CH_2OH , or CH_3 ; R^1 and R^2 are H, (C_1 - C_3) alkyl, or together form a cyclopropyl group with the carbon atom to which they are attached; n is 0 to 4; p is 0 or 1; R^3 is H or (C_1 - C_4) alkyl; Y is S, O, $NHCO$, $CONH$, or NH ; X is NH , O, S, SO , SO_2 , CO, or a single bond; and R^4 , R^5 , and R^6 are H, OH, halo, (C_1 - C_4) alkyl, (C_1 - C_4) alkoxy, nitro, (C_1 - C_4) alkylthio, amino, mono- or di- (C_1 - C_4) alkylamino, (C_1 - C_4) alkylsulfonyl, (C_1 - C_4) alkoxycarbonyl, (C_1 - C_4) alkylcarbonylamino, (C_1 - C_4) alkylsulfonylamino, $COOH$, $CONH_2$, CH_2OH , or phenyl; or a pharmaceutically acceptable salt thereof;

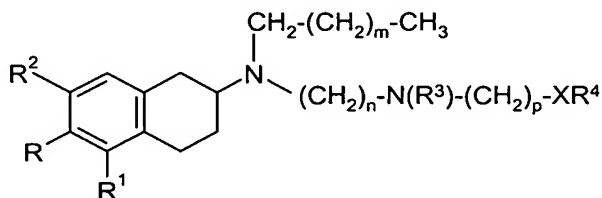
(g) a compound of Formula (0.0.6):



(0.0.6)

wherein A-D-E is $\text{CO}(\text{CH}_2)_p$; $\text{CH}(\text{OH})(\text{CH}_2)_p$; $\text{S}(\text{O})_m(\text{CH}_2)_2$; or $\text{S}(\text{O})_m\text{CH}=\text{CH}$; where p is 2 or 3, and m is 0, 1, or 2; X is CH_2 , or O when A-D-E does not contain S; n is 0 or 1 when X is CH_2 , or n is 1 when X is O; and R is H, $(\text{C}_1\text{-C}_{10})$ alkyl, $(\text{C}_3\text{-C}_{10})$ alkenyl, or $(\text{C}_3\text{-C}_{10})$ alkynyl each optionally substituted by $(\text{C}_3\text{-C}_8)$ cycloalkyl, phenyl, thienyl, or pyridyl, each optionally substituted by 1 to 3 of halo, OH, $(\text{C}_1\text{-C}_6)$ alkyl, or $(\text{C}_1\text{-C}_6)$ alkoxy; or a pharmaceutically acceptable salt thereof;

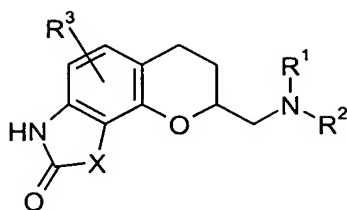
(h) a compound of Formula (0.0.8):



(0.0.8)

wherein R, R¹, and R² are H, or OH, provided at least one, but not all three thereof is hydrogen and provided R¹ and R² are not both OH; R³ is H or $(\text{C}_1\text{-C}_4)$ alkyl; R⁴ is phenyl, thienyl, imidazolyl, pyridyl, or isoxazolyl, each optionally substituted by halo, $(\text{C}_1\text{-C}_3)$ alkyl, or $(\text{C}_1\text{-C}_3)$ alkoxy; X is CH_2 ; NH; S; SO; SO₂; CO; CF₂; or O; or a direct bond when R⁴ is one of the above-recited 5- or 6-membered heterocyclyl residues; m is 1 or 2; and n is 3 to 8; or a pharmaceutically acceptable salt thereof;

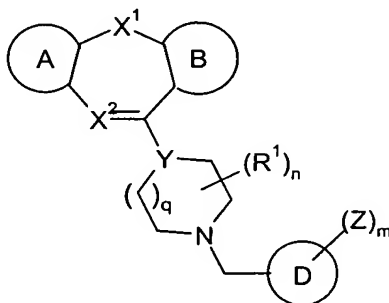
(i) a compound of Formula (0.0.9):



(0.0.9)

wherein X is $(\text{CH}_2)_n$ where n is 1 to 3; R^1 is $-\text{H}$; $(\text{C}_1\text{-C}_6)$ alkyl; hydroxy $(\text{C}_1\text{-C}_6)$ alkyl; cyclo $(\text{C}_3\text{-C}_7)$ alkylmethyl; bicyclo $(\text{C}_7\text{-C}_9)$ alkylmethyl; or $-(\text{CH}_2)_m\text{-Y-Ar}$ where m is 0 to 4, Y is CH_2 and Ar is phenyl; halophenyl; $(\text{C}_1\text{-C}_6)$ alkylphenyl; di $(\text{C}_1\text{-C}_6)$ alkylphenyl; or $(\text{C}_1\text{-C}_6)$ alkoxyphenyl; R^2 is H or $(\text{C}_1\text{-C}_6)$ alkyl; and R^3 is H; halo; $(\text{C}_1\text{-C}_6)$ alkyl; $(\text{C}_1\text{-C}_6)$ alkoxy; or hydroxy; or a pharmaceutically acceptable salt thereof;

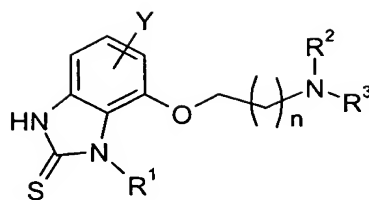
(j) a compound of Formula (0.0.10):



(0.0.10)

wherein A and B are benzene unsubstituted or substituted with 1 to 3 of OH, halo, $(\text{C}_1\text{-C}_4)$ alkyl, NH_2 , NO_2 , CN, halo substituted $(\text{C}_1\text{-C}_4)$ alkyl, halo substituted $(\text{C}_1\text{-C}_4)$ alkoxy, $(\text{C}_1\text{-C}_4)$ alkoxy, $(\text{C}_1\text{-C}_4)$ alkoxy, cyclo $(\text{C}_3\text{-C}_7)$ alkyl, $(\text{C}_1\text{-C}_4)$ alkylthio, tetrazolyl, N-piperidinyl, N-piperazinyl, N-morpholinyl, acetamido, $(\text{C}_1\text{-C}_4)$ alkylsulfonyl, sulfonamido, or OSO_3H ; X^1 is O, NH, N $-(\text{C}_1\text{-C}_4)$ alkyl, or N-acetyl; X^2 is N=; Y is CH or N; Z is cyano; R^1 is $(\text{C}_1\text{-C}_4)$ alkyl; m is 1 to 3; n is 0 to 2; q is 1 or 2; and D is benzene; or a pharmaceutically acceptable salt thereof;

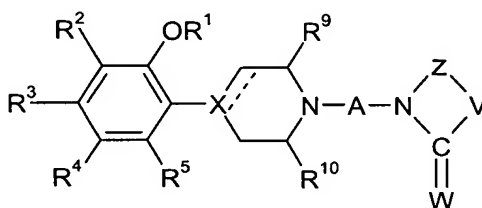
(k) a compound of Formula (0.0.12):



(0.0.12)

wherein R^1 is $-H$, or (C_1-C_6) alkyl; R^2 is $-H$, or (C_1-C_6) alkyl; R^3 is $-H$, straight or branched (C_1-C_{10}) alkyl, cyclohexylmethyl, or $-(CH_2)_mAr$ where m is 1 to 5, and Ar is phenyl, naphthyl, thienyl, furanyl, or pyridinyl, each substituted by 0 to 2 substituents independently selected from (C_1-C_6) alkyl, halo, (C_1-C_6) alkoxy, trifluoromethyl, and 4-fluorobutyrophenone; $-NR^2R^3$ is 1,2,3,4-tetrahydroquinolin-1-yl or 1,2,3,4-tetrahydroisoquinolin-2-yl; n is 1 or 2; and Y is halo, (C_1-C_6) alkyl, or (C_1-C_6) alkoxy; or a pharmaceutically acceptable salt thereof;

(I) a compound of Formula (0.0.13):

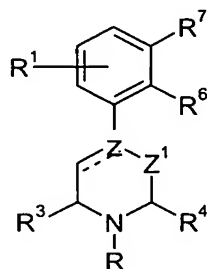


(0.0.13)

wherein A is (C_1-C_3) alkylene, or cyclo (C_3-C_7) alkylene; R^1 is (C_3-C_{10}) alkyl, cyclo (C_3-C_7) alkyl, cyclo (C_3-C_7) alkyl- (C_1-C_4) alkyl, trifluoromethylsulfonyl, or (C_1-C_4) alkylsulfonyl; R^2 to R^5 are H , halo, (C_1-C_4) alkyl, (C_1-C_4) alkoxy, (C_1-C_4) alkylthio, OH , (C_1-C_4) alkylsulfonyl, (C_1-C_4) alkylcarbonyl, CN , phenylcarbonyl, CF_3 , cyclo (C_3-C_7) alkyl, cyclo (C_3-C_7) alkyl- (C_1-C_4) alkyl, NO_2 , mono- or di- (C_1-C_4) alkylamino; R^9 and R^{10} are H , (C_1-C_4) alkyl, or together form an ethylene or propylene bridge; W is O or S ; V is O , S , CR^6R^7 , or NR^8 where R^6 , R^7 , and R^8 are H , (C_1-C_4) alkyl, cyclo (C_3-C_7) alkyl, (C_1-C_4) alkyl-phenyl, or phenyl, or R^6 and R^7 together constitute a 3-7 membered spiro-joined ring; Z is $-(CH_2)_m-$ where m is 2 or 3, or Z is $-$

CH=CH-; and the dashed line represents an optional bond such that when present, X is C, and when absent, X is N or CH; or a pharmaceutically acceptable salt thereof;

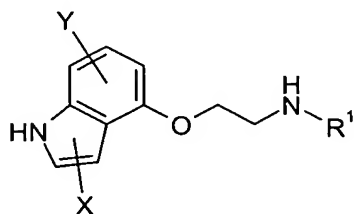
(m) a compound of Formula (0.0.14):



(0.0.14)

wherein R is $-\text{CH}_2\text{Z}^2\text{R}^5$; R^1 is $-\text{H}$ or $-\text{F}$; R^3 and R^4 are independently $-\text{H}$, or $(\text{C}_1\text{-C}_4)$ alkyl; R^5 is phenyl, furyl, or thienyl each substituted by 0 to 3 of $-\text{OH}$, halo, $(\text{C}_1\text{-C}_4)$ alkoxy, $(\text{C}_1\text{-C}_4)$ alkyl, $-\text{CN}$, $-\text{C}(=\text{O})\text{NH}_2$, or mono- or di- $(\text{C}_1\text{-C}_4)$ alkylaminocarbonyl; R^6 and R^7 are independently atoms that are necessary to complete a heterocyclic ring that is substituted by 0 to 2 of $(\text{C}_1\text{-C}_4)$ alkyl, $(\text{C}_1\text{-C}_4)$ alkoxy, or oxo; Z is $-\text{C}-$ or $-\text{N}-$; Z^1 is $-\text{CH}_2-$ or $-\text{CH}_2\text{CH}_2-$; Z^2 is 1,3-phenylene substituted by 0 to 3 of $-\text{OH}$, halo, $(\text{C}_1\text{-C}_4)$ alkoxy, or $(\text{C}_1\text{-C}_4)$ alkyl; the dashed line is a bond when Z is C and is absent when Z is N; or a pharmaceutically acceptable salt thereof;

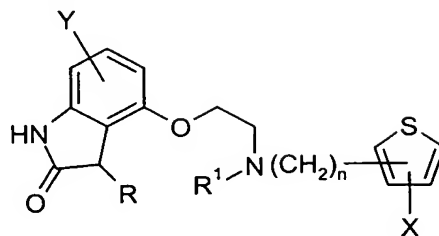
(n) a compound of Formula (0.0.16):



(0.0.16)

wherein R^1 is $(\text{C}_1\text{-C}_{10})$ alkyl, cyclo $(\text{C}_3\text{-C}_7)$ alkyl $(\text{C}_1\text{-C}_4)$ alkyl, phenyl $(\text{C}_1\text{-C}_4)$ alkyl, thienylmethyl, furanylmethyl, pyridinylmethyl, 4-fluorobutyrophenone, or 6-fluoro-1,2-benzisoxazolylpropyl; X is H, halo, CN, $(\text{C}_1\text{-C}_6)$ alkyl, acetyl, trifluoroacetyl, CF_3 , or formyl; and Y is H, halo, $(\text{C}_1\text{-C}_6)$ alkoxy, or $(\text{C}_1\text{-C}_6)$ alkyl; or a pharmaceutically acceptable salt thereof;

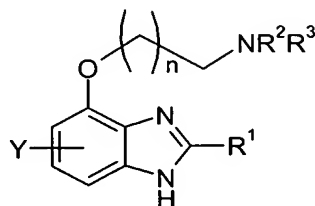
(o) a compound of Formula (0.0.18):



(0.0.18)

wherein Y is -H, halo, or -(C₁-C₄) alkoxy; R is -H, or -(C₁-C₄) alkylthio; R¹ is -H, or -(C₁-C₄) alkyl; X is -H, halo, -(C₁-C₄) alkyl, -(C₁-C₄) alkoxy, or phenyl; and n is 1-4; or a pharmaceutically acceptable salt thereof;

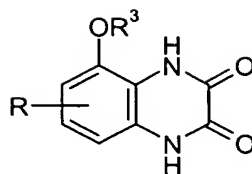
(p) a compound of Formula (0.0.19):



(0.0.19)

wherein R¹ is H, CF₃, C₂F₅, C₃F₇, (C₁-C₆) alkyl, or benzyl optionally substituted by 1 to 3 of halo, NH₂, NO₂, OH, or (C₁-C₆) alkoxy; R² is H or (C₁-C₆) alkyl; R³ is H, (C₁-C₁₀) alkyl, cyclohexylmethyl, or (CH₂)_mAr where Ar is phenyl, thienyl, furanyl, or pyridinyl optionally substituted by 1 or 2 of halo, (C₁-C₆) alkoxy, CF₃, or (C₁-C₆) alkyl; NR²R³ is 1,2,3,4-tetrahydroquinolin-1-yl, or 1,2,3,4-tetrahydroisoquinolin-2-yl; Y is halo, (C₁-C₆) alkyl, NH₂, or (C₁-C₆) alkoxy; and n is 1 to 5; or a pharmaceutically acceptable salt thereof;

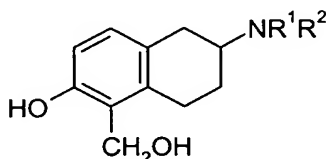
(q) a compound of Formula (0.0.20):



(0.0.20)

wherein R is halo, $-(C_1-C_4)$ alkyl, or $-(C_1-C_3)$ alkoxy; and R^3 is $-(CH_2)_nNR^1R^2$ where n is 1-2, and R^1 and R^2 are independently -H, $-(C_1-C_6)$ alkyl, or aryl(C_1-C_4) alkyl— where aryl is phenyl, naphthyl, or thienyl, or NR^1R^2 is 1,2,3,4-tetrahydroquinolin-1-yl, or 1,2,3,4-tetrahydroisoquinolin-2-yl; or a pharmaceutically acceptable salt thereof;

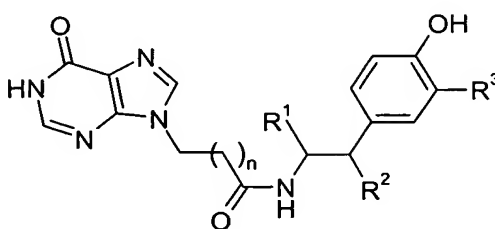
(r) a compound of Formula (0.0.21):



(0.0.21)

wherein R^1 and R^2 are independently -H, or $-(C_1-C_4)$ alkyl; or a pharmaceutically acceptable salt thereof;

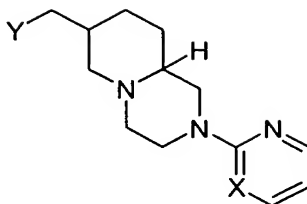
(s) a compound of Formula (0.0.22):



(0.0.22)

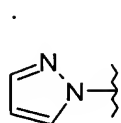
wherein R^1 is H or $C(=O)OR^4$; R^2 and R^3 are H or OH; R^4 is H, NH_2 , (C_1-C_4) alkyl, or (C_1-C_4) alkylamino; and n is 0 to 5; or a pharmaceutically acceptable salt thereof;

(t) a compound of Formula (0.0.23):

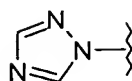


(0.0.23)

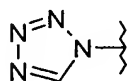
wherein X is N or CH; and Y is a moiety of partial Formulas (0.1.2) through (0.1.5):



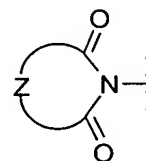
(0.1.2)



(0.1.3)

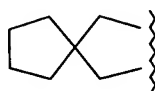


(0.1.4)

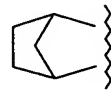


(0.1.5)

where Z is a moiety of partial Formulas (0.1.6) or (0.1.7):



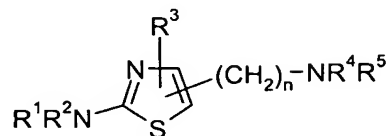
(0.1.6)



(0.1.7)

or Z is $-\text{SCH}_2-$, $-\text{OCH}_2-$, or $-\text{Y}^1(\text{CH}_2)_n-$, where n is 1 to 2, and Y^1 is $-\text{CH}_2-$, $-\text{NH}-$; or $-\text{N}(\text{CH}_3)-$; or a pharmaceutically acceptable salt thereof;

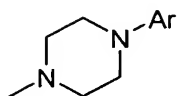
(u) a compound of Formula (0.0.24):



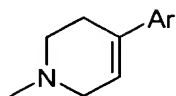
(0.0.24)

wherein n is 2 to 6; R^1 and R^2 are $-\text{H}$, (C_1-C_4) alkyl, phenyl, or (C_1-C_4) alkanoyl; R^3 is (C_1-C_4) alkyl, thienyl, or phenyl optionally substituted by halo, (C_1-C_4) alkyl, or (C_1-C_4) alkoxy; and NR^4R^5 is $-\text{NR}^6(\text{CH}_2\text{CH}_2\text{R}^7)$ where R^6 is $-\text{H}$ or $-(\text{C}_1-\text{C}_4)$ alkyl and R^7 is thienyl or phenyl optionally substituted by halo, (C_1-C_4) alkyl, or (C_1-C_4) alkoxy; or

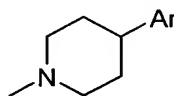
NR⁴R⁵ is Q¹, Q², or Q³, which are moieties of partial Formulas (0.1.8) through (0.1.10), respectively:



(0.1.8)



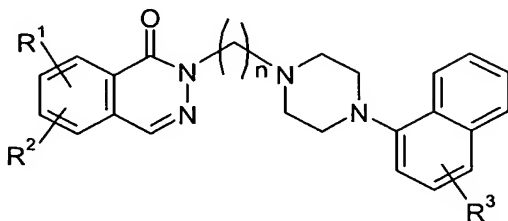
(0.1.9)



(0.1.10)

where Ar is pyridyl, pyrimidinyl, thienyl, or phenyl; or a pharmaceutically acceptable salt thereof;

(v) a compound of Formula (0.0.25):

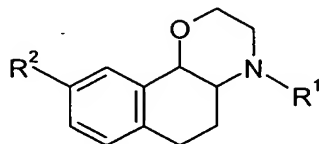


(0.0.25)

wherein R¹ and R² are H, (C₁-C₄) alkyl, halo, NO₂, NH₂, (C₁-C₄) alkanoylamino, or (C₁-C₄) alkoxy; n is 2 to 5; and R³ is H, OCH₃, or F; or a pharmaceutically acceptable salt thereof;

— and —

(w) a compound of Formula (0.0.26):



(0.0.26)

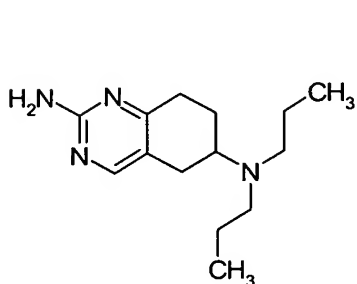
wherein R¹ is -(C₁-C₆) alkyl or -(C₃-C₆) alkenyl substituted by 0 to 2 of -(C₃-C₇) cycloalkyl, phenyl, thienyl, or pyridyl, each substituted in turn by 0 to 2 of halo, -OH, -(C₁-C₄) alkyl, or -(C₁-C₄) alkoxy; and R² is -CN, -C(=O)CH₃, -C(=O)NR³R⁴, or -

C(=O)R³, where R³ and R⁴ are -H, or -(C₁-C₄) alkyl; or a pharmaceutically acceptable salt thereof.

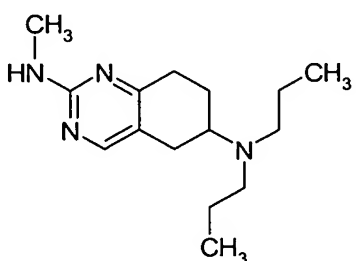
4. The composition according to Claim 3 wherein the dopamine D2-receptor agonist is a member selected from the group consisting of alentemol hydrobromide; apomorphine hydrochloride; bromocriptine mesylate; cabergoline; fenoldopam mesylate; levodopa; lisuride; naxagolide hydrochloride; pergolide mesylate; pramipexole dihydrochloride; quinpirole hydrochloride; ropinirole hydrochloride; and talipexole.

5. The composition according to Claim 3 wherein the dopamine D2-receptor agonist is:

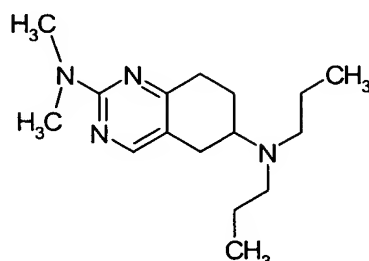
- of the type in Formula (0.0.1) represented by Formulas (0.5.1) through (0.5.3):



(0.5.1)

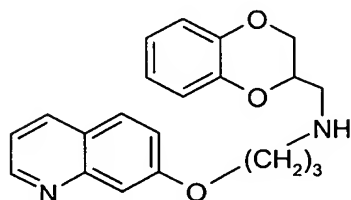


(0.5.2)

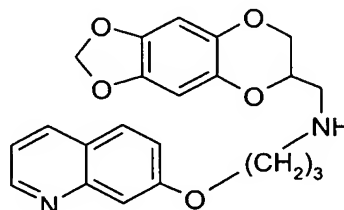


(0.5.3)

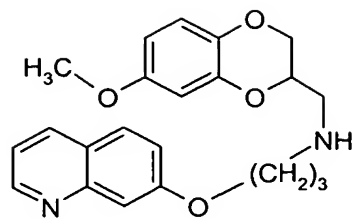
- of the type in Formula (0.0.2) represented by Formulas (0.5.4) through (0.5.8):



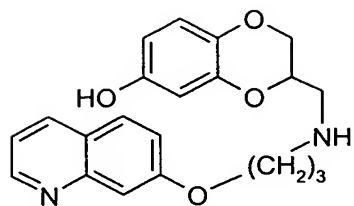
(0.5.4)



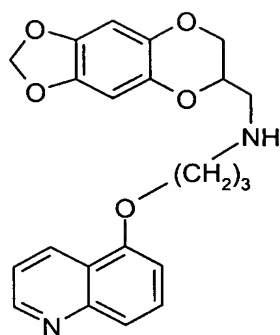
(0.5.5)



(0.5.6)

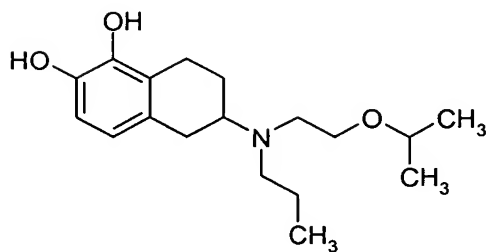


(0.5.7)

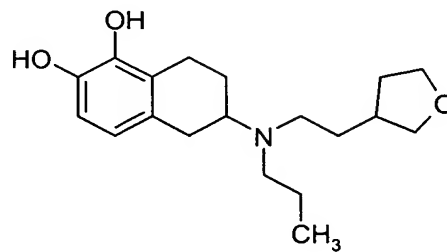


(0.5.8)

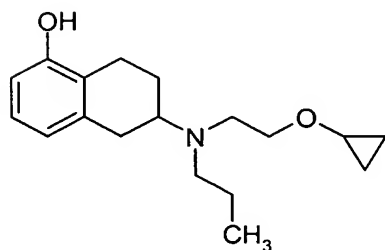
- of the type in Formula (0.0.3) represented by Formulas (0.5.9) through (0.5.14):



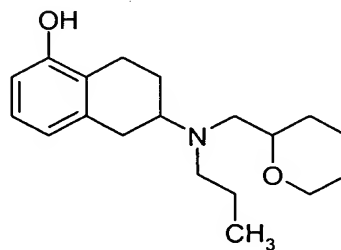
(0.5.9)



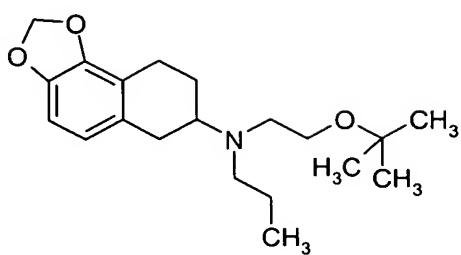
(0.5.10)



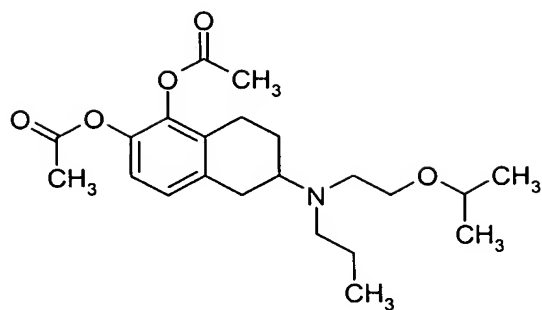
(0.5.11)



(0.5.12)

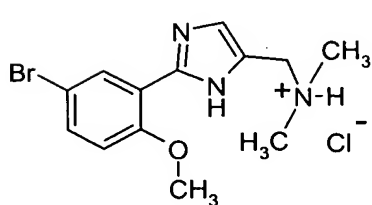


(0.5.13)

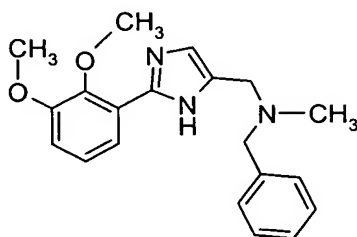


(0.5.14)

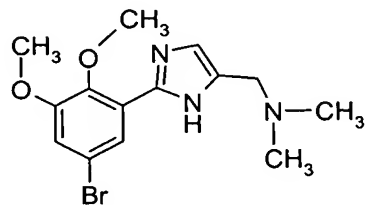
- of the type in Formula (0.0.4) represented by Formulas (0.5.15) through (0.5.21):



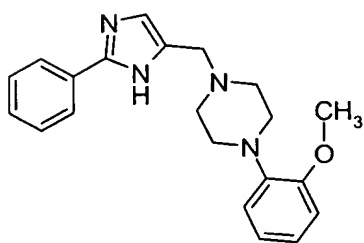
(0.5.15)



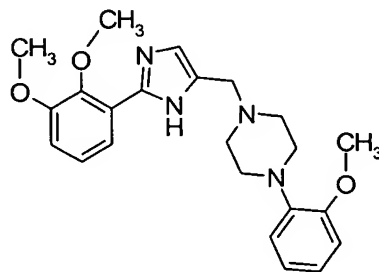
(0.5.16)



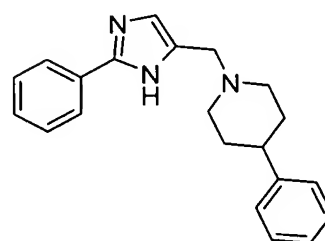
(0.5.17)



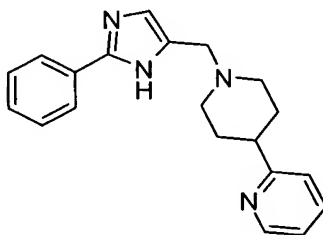
(0.5.18)



(0.5.19)

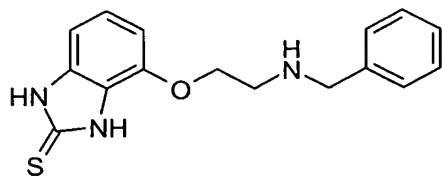


(0.5.20)

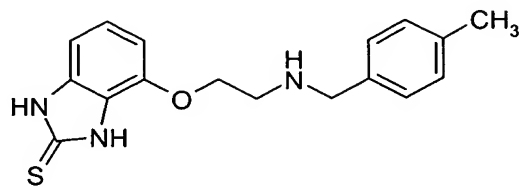


(0.5.21)

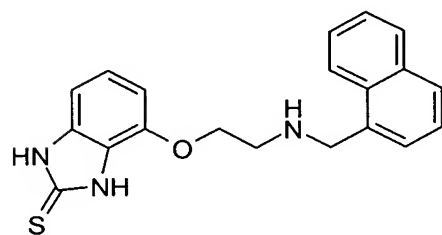
- of the type in Formula (0.0.12) represented by Formulas (0.5.22) through (0.5.27):



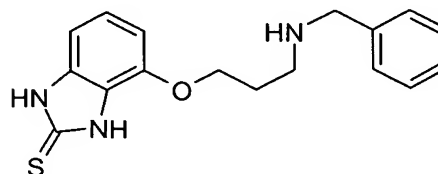
(0.5.22)



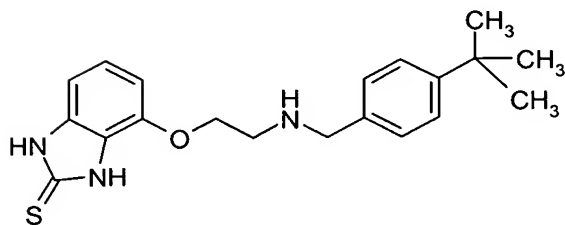
(0.5.23)



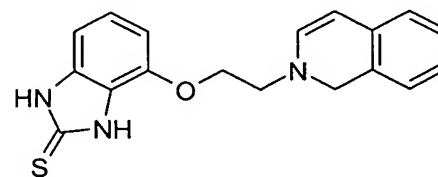
(0.5.24)



(0.5.25)

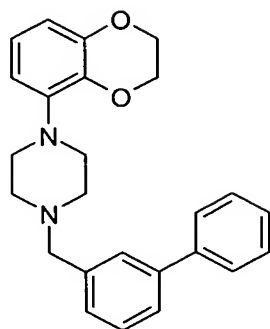


(0.5.26)

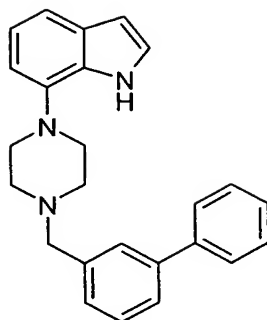


(0.5.27)

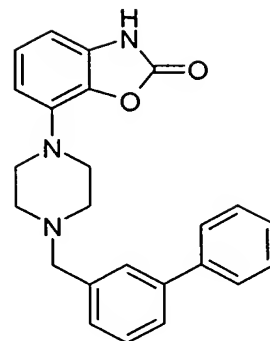
- of the type in Formula (0.0.14) represented by Formulas (0.5.28) through (0.5.30):



(0.5.28)

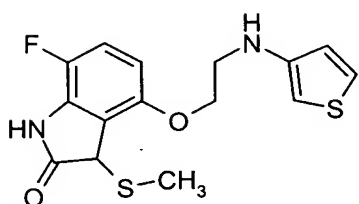


(0.5.29)

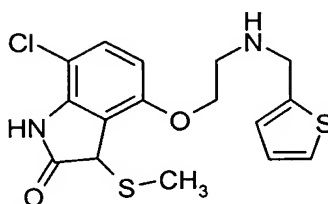


(0.5.30)

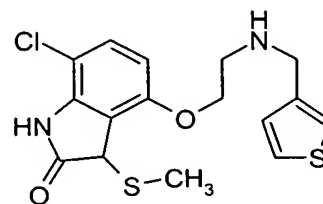
- of the type in Formula (0.0.18) represented by Formulas (0.5.31) through (0.5.35):



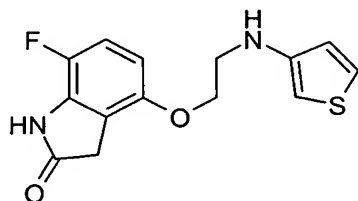
(0.5.31)



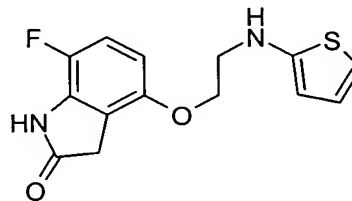
(0.5.32)



(0.5.33)

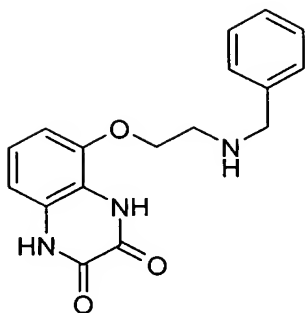


(0.5.34)

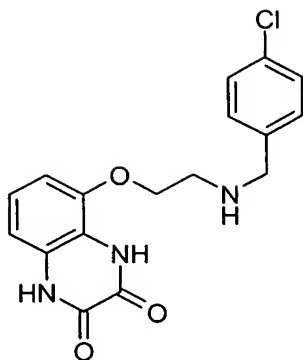


(0.5.35)

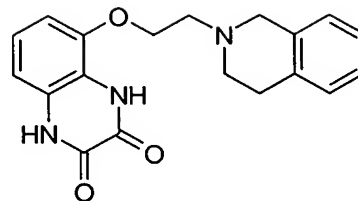
- of the type in Formula (0.0.20) represented by Formulas (0.5.36) through (0.5.38):



(0.5.36)

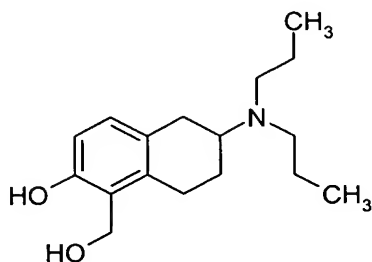


(0.5.37)



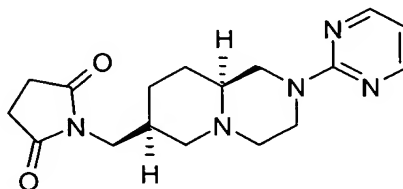
(0.5.38)

- of the type in Formula (0.0.21) represented by Formula (0.5.39):



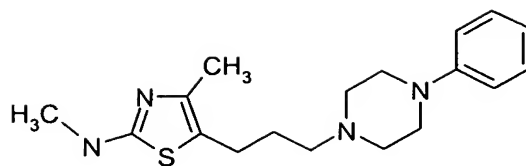
(0.5.39)

- of the type in Formula (0.0.23) represented by Formula (0.5.40):



(0.5.40)

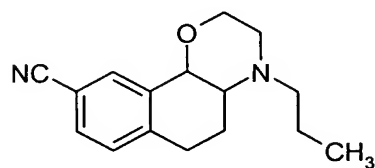
- of the type in Formula (0.0.24) represented by Formula (0.5.41):



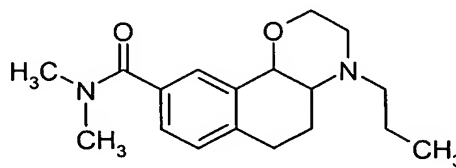
(0.5.41)

— or —

- of the type in Formula (0.0.26) represented by Formulas (0.5.42) through (0.5.43):

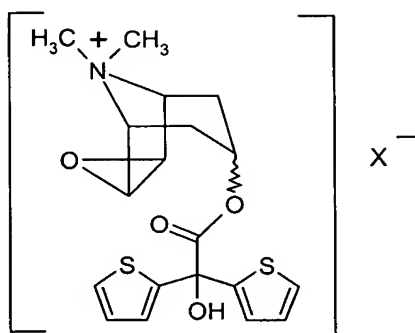


(0.5.42)



(0.5.43)

6. The composition according to Claim 1 wherein the anti-cholinergic agent comprises a compound of Formula (1.1.1):



(1.1.1)

wherein X^- is a physiologically acceptable anion.

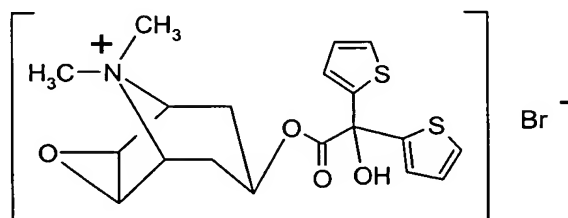
7. The composition according to Claim 6 wherein the physiologically acceptable anion, X^- , is a member selected from the group consisting of fluoride, F^- ;

chloride, Cl^- ; bromide, Br^- ; iodide, I^- ; methanesulfonate, $\text{CH}_3\text{S}(=\text{O})_2\text{O}^-$; ethanesulfonate, $\text{CH}_3\text{CH}_2\text{S}(=\text{O})_2\text{O}^-$; methylsulfate, $\text{CH}_3\text{OS}(=\text{O})_2\text{O}^-$; benzene sulfonate, $\text{C}_6\text{H}_5\text{S}(=\text{O})_2\text{O}^-$; *p*-toluenesulfonate, and $4\text{-CH}_3\text{-C}_6\text{H}_4\text{S}(=\text{O})_2\text{O}^-$.

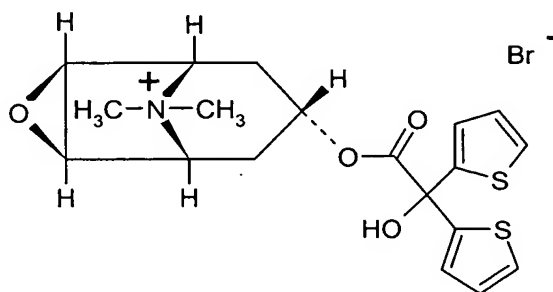
8. The composition according to Claim 7 wherein the physiologically acceptable anion, X^- , is bromide, Br^- .

9. The composition according to Claim 6 wherein the anti-cholinergic agent comprises a 3- α compound.

10. The composition according to Claim 9 wherein the anticholinergic agent is comprises tiotropium bromide, $(1\alpha, 2\beta, 4\beta, 5\alpha, 7\beta)$ -7-[(hydroxydi-2-thienylacetyl)oxy]-9,9-dimethyl-3-oxa-9-azoniatricyclo[3.3.1.0^{2,4}]nonane bromide, represented by Formula (1.1.2) or Formula (1.1.3):



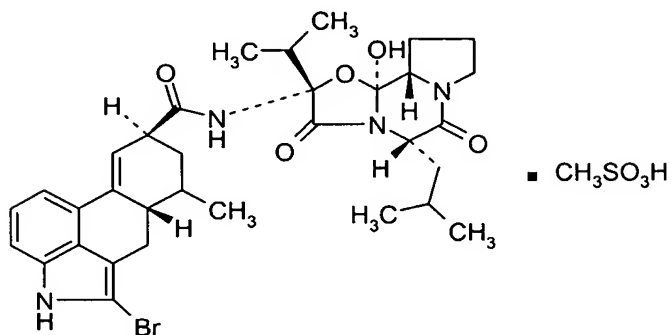
(1.1.2)



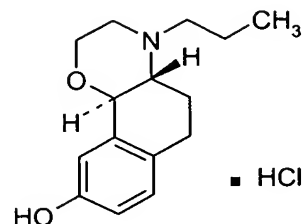
(1.1.3)

11. The composition according to Claim 1 wherein:

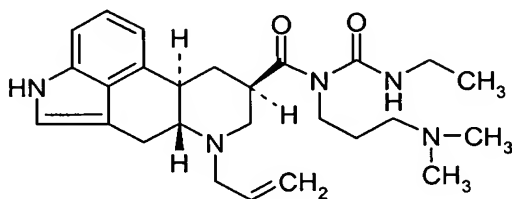
(a) the dopamine D2-receptor agonist is a member selected from the group consisting of:



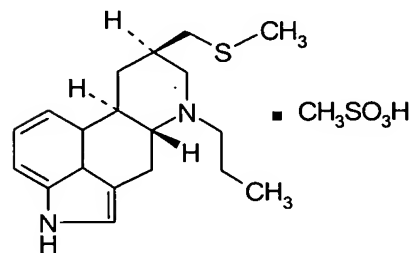
bromocriptine mesylate



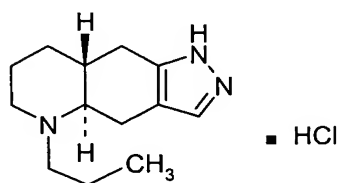
naxagolide hydrochloride



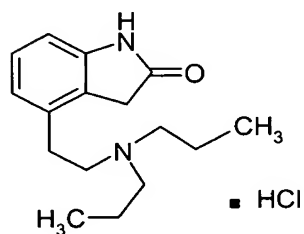
cabergoline



pergolide mesylate



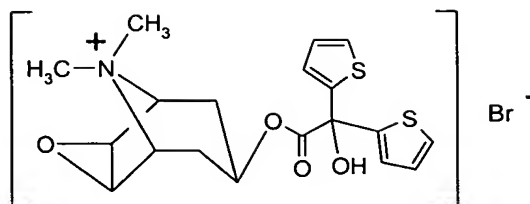
quinpirole hydrochloride



ropinirole hydrochloride

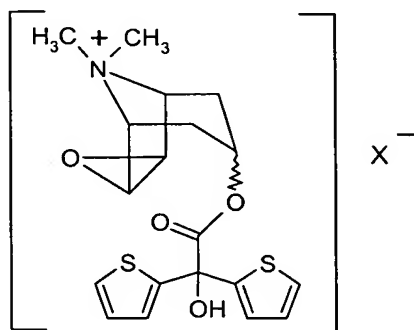
— and —

(b) the anti-cholinergic agent comprises tiotropium bromide of Formula (1.1.2):



(1.1.2)

12. A method for the treatment of obstructive airways or other inflammatory diseases in a mammal comprising administering to the mammal a therapeutically effective amount of a composition comprising (I) a dopamine D2-receptor agonist and (II) an anti-cholinergic agent comprising a compound of Formula (1.1.1):



(1.1.1)

wherein X^- is a physiologically acceptable anion.

13. The method according to Claim 12 wherein the obstructive airways disease is asthma, COPD, or other obstructive airways disease exacerbated by bronchial hyper-reactivity and bronchospasm.

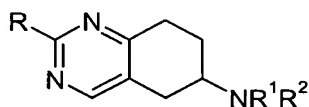
14. The method according to Claim 13 wherein the mammal is a human being.

15. The method according to Claim 14 comprising simultaneous or sequential delivery of the dopamine D2-receptor agonist and anti-cholinergic agent in the form of an aerosol or dry powder by inhalation.

16. The method according to Claim 15 wherein the dopamine D2-receptor agonist comprises:

(a) alentemol; apomorphine; biperiden; bromocriptine; cabergoline; carmoxirole; ciladopa; dopexamine; fenoldopam; ibopamine; levodopa; lisuride; methylenedioxypromethazine; naxagolide; *N*-allylnorapomorphine; pergolide; pramipexole; propylnorapomorphine; protokylol; quinagolide; quinpirole; ropinirole; roxindole; talipexole; terguride; trihexyphenidyl; and trihydroxyapomorphine and salts and combinations thereof;

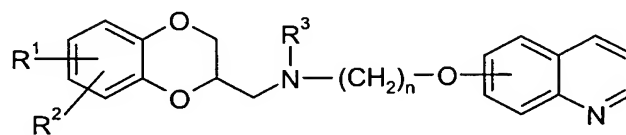
(b) a compound of Formula (0.0.1):



(0.0.1)

wherein R is -H, -OH, (C₁-C₄) alkylcarbonyloxy-, (C₁-C₄) alkylthio-, or -NR^aR^b where R^a and R^b are independently -H, -CH₃, -CH₂CH₃, or *n*-propyl; and R¹ and R² are independently -CH₃, -CH₂CH₃, *n*-propyl, or allyl; or a pharmaceutically acceptable salt thereof;

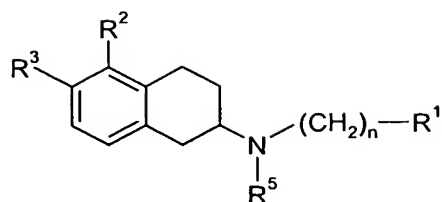
(c) a compound of Formula (0.0.2):



(0.0.2)

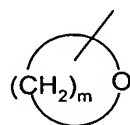
wherein n is 2-4; R¹ and R² are independently -H, -(C₁-C₆) alkyl, -(C₁-C₆) alkoxy, -(C₇-C₁₂) arylalkoxy, -(C₂-C₆) alkanoyloxy, -OH, halo, -NH₂, mono- or di-(C₁-C₆) alkylamino; -(C₂-C₆) alkanamido; or sulfonamido; R³ is -H, or -(C₁-C₆) alkyl; or R¹R² together are methylenedioxy, ethylenedioxy, or propylenedioxy; or a pharmaceutically acceptable salt thereof;

(d) a compound of Formula (0.0.3):



(0.0.3)

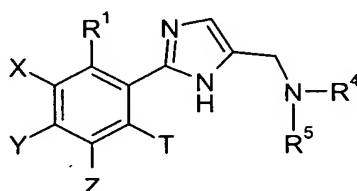
wherein R^2 is OA; and R^3 is $-H$ or OA; where A is $-H$, a hydrocarbyl radical of 1 to 3 carbon atoms, $-C(=O)R^4$, $-C(=O)NHR^4$, $-C(=O)N(R^4)_2$, or $-C(=O)OR^4$; provided that when R^2 and R^3 are OA, then R^2 and R^3 may be bonded together to form $-O-CH_2-O-$, or $-O-C(=O)-O-$; R^4 is (C_1-C_6) alkyl or an aromatic residue of 1-20 carbon atoms; n is 1-4; R^5 is unbranched (C_1-C_3) alkyl, or cyclopropylmethyl; and R^1 is (C_1-C_3) alkoxy, (C_3-C_6) cycloalkoxy, or a cyclic ether of partial Formula (0.1.1):



(0.1.1)

where m is 3 to 5; provided that when R^1 is (C_1-C_3) alkoxy, then R^3 cannot be $-H$; or a pharmaceutically acceptable salt thereof;

(e) a compound of Formula (0.0.4):

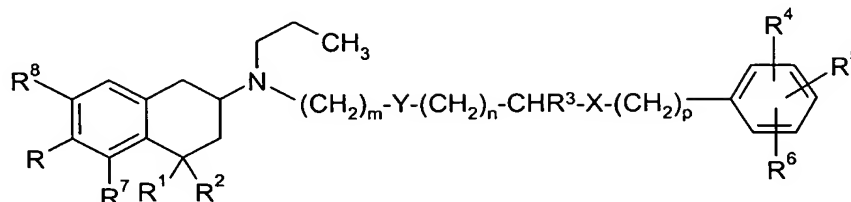


(0.0.4)

wherein R^1 and T are $-H$; halo; $-OH$; straight or branched (C_1-C_6) alkyl; or straight or branched (C_1-C_6) alkoxy; X and Z have the same meaning as R^1 and T additionally including SO_2R^6 where R^6 is straight or branched (C_1-C_6) alkyl; Y is $-H$; halo; $-NH_2$; or straight or branched (C_1-C_6) alkyl; R^4 and R^5 are $-H$; straight or branched (C_1-C_6) alkyl; phenyl (C_1-C_6) alkyl; or pyridyl (C_1-C_6) alkyl; and $-NR^4R^5$ is 2-(1,2,3,4-tetrahydroisoquinolinyl) substituted by 0 to 2 of halo; $-OH$; straight or branched

(C₁-C₆) alkyl; or straight or branched (C₁-C₆) alkoxy; or a pharmaceutically acceptable salt thereof;

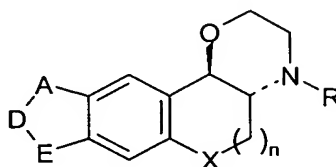
(f) a compound of Formula (0.0.5):



(0.0.5)

wherein m is 4 to 8; R, R⁷, and R⁸ are H or OH, provided at least one is H but not all three are H and provided R⁷ and R⁸ are not both OH, or one of R⁷ and R⁸ is H and the other is NHCHO, NHCH₃, NHSO₂CH₃, CH₂OH, or CH₃; R¹ and R² are H, (C₁-C₃) alkyl, or together form a cyclopropyl group with the carbon atom to which they are attached; n is 0 to 4; p is 0 or 1; R³ is H or (C₁-C₄) alkyl; Y is S, O, NHCO, CONH, or NH; X is NH, O, S, SO, SO₂, CO, or a single bond; and R⁴, R⁵, and R⁶ are H, OH, halo, (C₁-C₄) alkyl, (C₁-C₄) alkoxy, nitro, (C₁-C₄) alkylthio, amino, mono- or di-(C₁-C₄) alkylamino, (C₁-C₄) alkylsulfonyl, (C₁-C₄) alkoxycarbonyl, (C₁-C₄) alkylcarbonylamino, (C₁-C₄) alkylsulfonylamino, COOH, CONH₂, CH₂OH, or phenyl; or a pharmaceutically acceptable salt thereof;

(g) a compound of Formula (0.0.6):

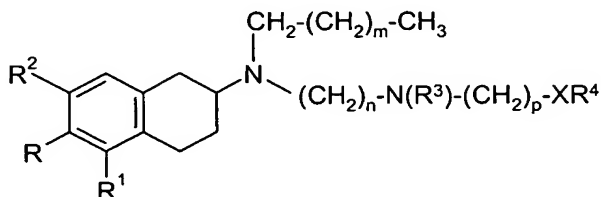


(0.0.6)

wherein A-D-E is CO(CH₂)_p; CH(OH)(CH₂)_p; S(O)_m(CH₂)₂; or S(O)_mCH=CH; where p is 2 or 3, and m is 0, 1, or 2; X is CH₂, or O when A-D-E does not contain S; n is 0 or 1 when X is CH₂, or n is 1 when X is O; and R is H, (C₁-C₁₀) alkyl, (C₃-C₁₀) alkenyl, or (C₃-C₁₀) alkynyl each optionally substituted by (C₃-C₈) cycloalkyl,

phenyl, thienyl, or pyridyl, each optionally substituted by 1 to 3 of halo, OH, (C₁-C₆) alkyl, or (C₁-C₆) alkoxy; or a pharmaceutically acceptable salt thereof;

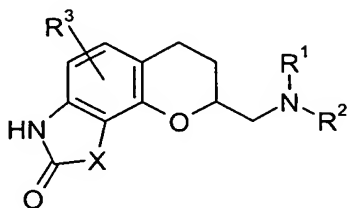
(h) a compound of Formula (0.0.8):



(0.0.8)

wherein R, R¹, and R² are H, or OH, provided at least one, but not all three thereof is hydrogen and provided R¹ and R² are not both OH; R³ is H or (C₁-C₄) alkyl; R⁴ is phenyl, thienyl, imidazolyl, pyridyl, or isoxazolyl, each optionally substituted by halo, (C₁-C₃) alkyl, or (C₁-C₃) alkoxy; X is CH₂; NH; S; SO; SO₂; CO; CF₂; or O; or a direct bond when R⁴ is one of the above-recited 5- or 6-membered heterocyclyl residues; m is 1 or 2; and n is 3 to 8; or a pharmaceutically acceptable salt thereof;

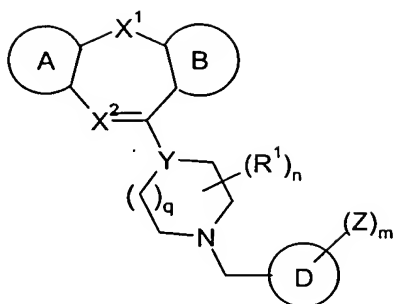
(i) a compound of Formula (0.0.9):



(0.0.9)

wherein X is (CH₂)_n where n is 1 to 3; R¹ is -H; (C₁-C₆) alkyl; hydroxy(C₁-C₆) alkyl; cyclo(C₃-C₇) alkylmethyl; bicyclo(C₇-C₉) alkylmethyl; or - (CH₂)_m-Y-Ar where m is 0 to 4, Y is CH₂ and Ar is phenyl; halophenyl; (C₁-C₆) alkylphenyl; di-(C₁-C₆) alkylphenyl; or (C₁-C₆) alkoxyphenyl; R² is H or (C₁-C₆) alkyl; and R³ is H; halo; (C₁-C₆) alkyl; (C₁-C₆) alkoxy; or hydroxy; or a pharmaceutically acceptable salt thereof;

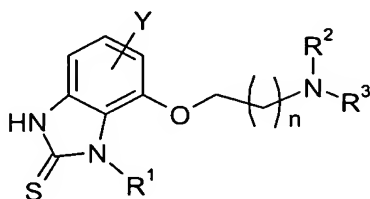
(j) a compound of Formula (0.0.10):



(0.0.10)

wherein A and B are benzene unsubstituted or substituted with 1 to 3 of OH, halo, (C₁-C₄) alkyl, NH₂, NO₂, CN, halo substituted (C₁-C₄) alkyl, halo substituted (C₁-C₄) alkoxy, (C₁-C₄) alkoxycarbonyl, cyclo(C₃-C₇) alkyl, (C₁-C₄) alkylthio, tetrazolyl, N-piperidinyl, N-piperazinyl, N-morpholinyl, acetamido, (C₁-C₄) alkylsulfonyl, sulfonamido, or OSO₃H; X¹ is O, NH, N-(C₁-C₄) alkyl, or N-acetyl; X² is N=; Y is CH or N; Z is cyano; R¹ is (C₁-C₄) alkyl; m is 1 to 3; n is 0 to 2; q is 1 or 2; and D is benzene; or a pharmaceutically acceptable salt thereof;

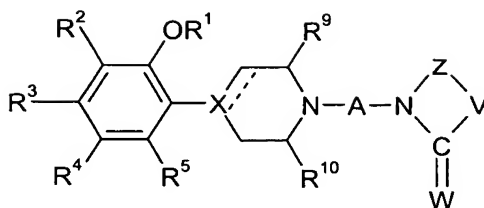
(k) a compound of Formula (0.0.12):



(0.0.12)

wherein R¹ is -H, or (C₁-C₆) alkyl; R² is -H, or (C₁-C₆) alkyl; R³ is -H, straight or branched (C₁-C₁₀) alkyl, cyclohexylmethyl, or -(CH₂)_mAr where m is 1 to 5, and Ar is phenyl, naphthyl, thienyl, furanyl, or pyridinyl, each substituted by 0 to 2 substituents independently selected from (C₁-C₆) alkyl, halo, (C₁-C₆) alkoxy, trifluoromethyl, and 4-fluorobutyrophenone; -NR²R³ is 1,2,3,4-tetrahydroquinolin-1-yl or 1,2,3,4-tetrahydroisoquinolin-2-yl; n is 1 or 2; and Y is halo, (C₁-C₆) alkyl, or (C₁-C₆) alkoxy; or a pharmaceutically acceptable salt thereof;

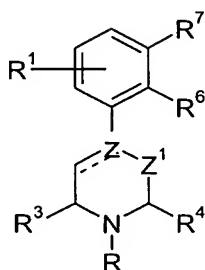
(l) a compound of Formula (0.0.13):



(0.0.13)

wherein A is (C₁-C₃) alkylene, or cyclo(C₃-C₇) alkylene; R¹ is (C₃-C₁₀) alkyl, cyclo(C₃-C₇) alkyl, cyclo(C₃-C₇) alkyl-(C₁-C₄) alkyl, trifluoromethylsulfonyl, or (C₁-C₄) alkylsulfonyl; R² to R⁵ are H, halo, (C₁-C₄) alkyl, (C₁-C₄) alkoxy, (C₁-C₄) alkylthio, OH, (C₁-C₄) alkylsulfonyl, (C₁-C₄) alkylcarbonyl, CN, phenylcarbonyl, CF₃, cyclo(C₃-C₇) alkyl, cyclo(C₃-C₇) alkyl-(C₁-C₄) alkyl, NO₂, mono- or di-(C₁-C₄) alkylamino; R⁹ and R¹⁰ are H, (C₁-C₄) alkyl, or together form an ethylene or propylene bridge; W is O or S; V is O, S, CR⁶R⁷, or NR⁸ where R⁶, R⁷, and R⁸ are H, (C₁-C₄) alkyl, cyclo(C₃-C₇) alkyl, (C₁-C₄) alkyl-phenyl, or phenyl, or R⁶ and R⁷ together constitute a 3-7 membered spiro-joined ring; Z is -(CH₂)_m- where m is 2 or 3, or Z is -CH=CH-; and the dashed line represents an optional bond such that when present, X is C, and when absent, X is N or CH; or a pharmaceutically acceptable salt thereof;

(m) a compound of Formula (0.0.14):

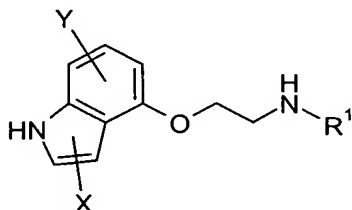


(0.0.14)

wherein R is -CH₂Z²R⁵; R¹ is -H or -F; R³ and R⁴ are independently -H, or (C₁-C₄) alkyl; R⁵ is phenyl, furyl, or thienyl each substituted by 0 to 3 of -OH, halo, (C₁-C₄) alkoxy, (C₁-C₄) alkyl, -CN, -C(=O)NH₂, or mono- or di-(C₁-C₄) alkylaminocarbonyl; R⁶ and R⁷ are independently atoms that are necessary to complete a heterocyclic ring that is substituted by 0 to 2 of (C₁-C₄) alkyl, (C₁-C₄) alkoxy, or oxo; Z is -C- or -N-; Z¹ is -CH₂- or -CH₂CH₂-; Z² is 1,3-phenylene substituted by 0

to 3 of –OH, halo, (C₁-C₄) alkoxy, or (C₁-C₄) alkyl; the dashed line is a bond when Z is C and is absent when Z is N; or a pharmaceutically acceptable salt thereof;

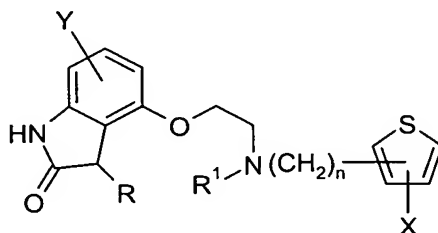
(n) a compound of Formula (0.0.16):



(0.0.16)

wherein R¹ is (C₁-C₁₀) alkyl, cyclo(C₃-C₇) alkyl(C₁-C₄) alkyl, phenyl(C₁-C₄) alkyl, thienylmethyl, furanylmethyl, pyridinylmethyl, 4-fluorobutyrophenone, or 6-fluoro-1,2-benzisoxazolylpropyl; X is H, halo, CN, (C₁-C₆) alkyl, acetyl, trifluoroacetyl, CF₃, or formyl; and Y is H, halo, (C₁-C₆) alkoxy, or (C₁-C₆) alkyl; or a pharmaceutically acceptable salt thereof;

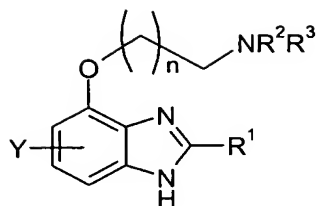
(o) a compound of Formula (0.0.18):



(0.0.18)

wherein Y is –H, halo, or –(C₁-C₄) alkoxy; R is –H, or –(C₁-C₄) alkylthio; R¹ is –H, or –(C₁-C₄) alkyl; X is –H, halo, –(C₁-C₄) alkyl, –(C₁-C₄) alkoxy, or phenyl; and n is 1-4; or a pharmaceutically acceptable salt thereof;

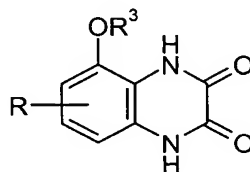
(p) a compound of Formula (0.0.19):



(0.0.19)

wherein R^1 is H, CF_3 , C_2F_5 , C_3F_7 , (C_1-C_6) alkyl, or benzyl optionally substituted by 1 to 3 of halo, NH_2 , NO_2 , OH , or (C_1-C_6) alkoxy; R^2 is H or (C_1-C_6) alkyl; R^3 is H, (C_1-C_{10}) alkyl, cyclohexylmethyl, or $(CH_2)_mAr$ where Ar is phenyl, thienyl, furanyl, or pyridinyl optionally substituted by 1 or 2 of halo, (C_1-C_6) alkoxy, CF_3 , or (C_1-C_6) alkyl; NR^2R^3 is 1,2,3,4-tetrahydroquinolin-1-yl, or 1,2,3,4-tetrahydroisoquinolin-2-yl; Y is halo, (C_1-C_6) alkyl, NH_2 , or (C_1-C_6) alkoxy; and n is 1 to 5; or a pharmaceutically acceptable salt thereof;

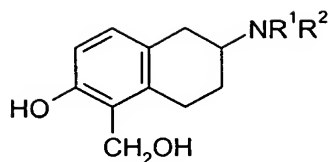
(q) a compound of Formula (0.0.20):



(0.0.20)

wherein R is halo, $-(C_1-C_4)$ alkyl, or $-(C_1-C_3)$ alkoxy; and R^3 is $-(CH_2)_nNR^1R^2$ where n is 1-2, and R^1 and R^2 are independently -H, $-(C_1-C_6)$ alkyl, or aryl (C_1-C_4) alkyl—where aryl is phenyl, naphthyl, or thienyl, or NR^1R^2 is 1,2,3,4-tetrahydroquinolin-1-yl, or 1,2,3,4-tetrahydroisoquinolin-2-yl; or a pharmaceutically acceptable salt thereof;

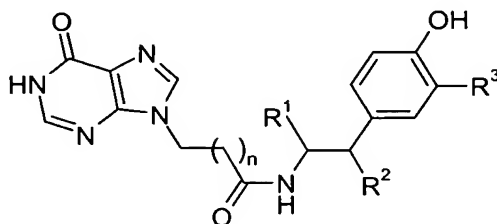
(r) a compound of Formula (0.0.21):



(0.0.21)

wherein R¹ and R² are independently -H, or -(C₁-C₄) alkyl; or a pharmaceutically acceptable salt thereof;

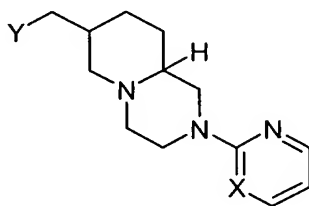
(s) a compound of Formula (0.0.22):



(0.0.22)

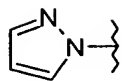
wherein R¹ is H or C(=O)OR⁴; R² and R³ are H or OH; R⁴ is H, NH₂, (C₁-C₄) alkyl, or (C₁-C₄) alkylamino; and n is 0 to 5; or a pharmaceutically acceptable salt thereof;

(t) a compound of Formula (0.0.23):

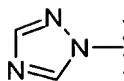


(0.0.23)

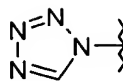
wherein X is N or CH; and Y is a moiety of partial Formulas (0.1.2) through (0.1.5):



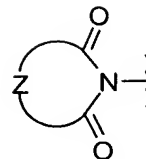
(0.1.2)



(0.1.3)

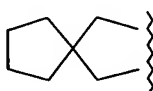


(0.1.4)

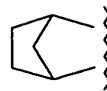


(0.1.5)

where Z is a moiety of partial Formulas (0.1.6) or (0.1.7):



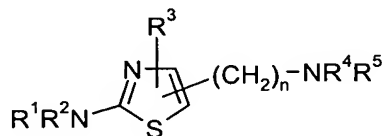
(0.1.6)



(0.1.7)

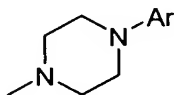
or Z is $-\text{SCH}_2-$, $-\text{OCH}_2-$, or $-\text{Y}^1(\text{CH}_2)_n-$, where n is 1 to 2, and Y^1 is $-\text{CH}_2-$, $-\text{NH}-$, or $-\text{N}(\text{CH}_3)-$; or a pharmaceutically acceptable salt thereof;

(u) a compound of Formula (0.0.24):

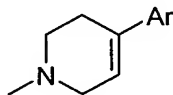


(0.0.24)

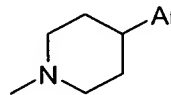
wherein n is 2 to 6; R^1 and R^2 are $-\text{H}$, $(\text{C}_1\text{-C}_4)$ alkyl, phenyl, or $(\text{C}_1\text{-C}_4)$ alkanoyl; R^3 is $(\text{C}_1\text{-C}_4)$ alkyl, thienyl, or phenyl optionally substituted by halo, $(\text{C}_1\text{-C}_4)$ alkyl, or $(\text{C}_1\text{-C}_4)$ alkoxy; and NR^4R^5 is $-\text{NR}^6(\text{CH}_2\text{CH}_2\text{R}^7)$ where R^6 is $-\text{H}$ or $-(\text{C}_1\text{-C}_4)$ alkyl and R^7 is thienyl or phenyl optionally substituted by halo, $(\text{C}_1\text{-C}_4)$ alkyl, or $(\text{C}_1\text{-C}_4)$ alkoxy; or NR^4R^5 is Q^1 , Q^2 , or Q^3 , which are moieties of partial Formulas (0.1.8) through (0.1.10), respectively:



(0.1.8)



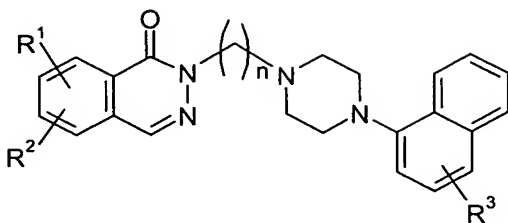
(0.1.9)



(0.1.10)

where Ar is pyridyl, pyrimidinyl, thienyl, or phenyl; or a pharmaceutically acceptable salt thereof;

(v) a compound of Formula (0.0.25):

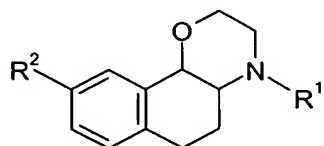


(0.0.25)

wherein R¹ and R² are H, (C₁-C₄) alkyl, halo, NO₂, NH₂, (C₁-C₄) alkanoylamino, or (C₁-C₄) alkoxy; n is 2 to 5; and R³ is H, OCH₃, or F; or a pharmaceutically acceptable salt thereof;

— and —

(w) a compound of Formula (0.0.26):



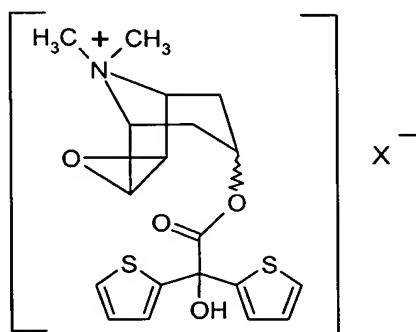
(0.0.26)

wherein R¹ is -(C₁-C₆) alkyl or -(C₃-C₆) alkenyl substituted by 0 to 2 of -(C₃-C₇) cycloalkyl, phenyl, thienyl, or pyridyl, each substituted in turn by 0 to 2 of halo, -OH, -(C₁-C₄) alkyl, or -(C₁-C₄) alkoxy; and R² is -CN, -C(=O)CH₃, -C(=O)NR³R⁴, or -C(=O)R³, where R³ and R⁴ are -H, or -(C₁-C₄) alkyl; or a pharmaceutically acceptable salt thereof.

17. The method according to Claim 16 wherein the dopamine D2-receptor agonist is selected from the group consisting of alentemol hydrobromide; apomorphine hydrochloride; bromocriptine mesylate; cabergoline; fenoldopam mesylate; levodopa; lisuride; naxagolide hydrochloride; pergolide mesylate; pramipexole dihydrochloride; quinpirole hydrochloride; ropinirole hydrochloride; and talipexole.

18. The method according to Claim 17 wherein said dopamine D2-receptor agonist is selected from the group consisting of bromocriptine mesylate, naxagolide hydrochloride, cabergoline, pergolide mesylate, quinpirole hydrochloride, and ropinirole hydrochloride.

19. The method according to Claim 15 wherein the anti-cholinergic agent comprises a compound of Formula (1.1.1):



(1.1.1)

wherein X⁻ is a physiologically acceptable anion.

20. The composition according to claim 1 comprising (I) a dopamine D2-receptor agonist and (II) an anti-cholinergic agent, in an effective therapeutic amount to treat inflammatory disease or obstructive airways disease, in a form suitable for administration by inhalation.

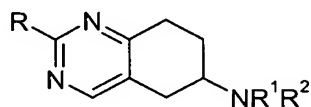
21. The composition according to Claim 20 wherein the obstructive airways disease is asthma, COPD, or other obstructive airways disease exacerbated by bronchial hyper-reactivity and bronchospasm.

22. The composition according to Claim 20 wherein the form suitable for administration by inhalation comprises simultaneous or sequential delivery of components (I) and (II) in the form of an aerosol or dry powder.

23. The composition according to Claim 20 wherein the dopamine D2-receptor agonist comprises a member selected from the group consisting of:

(a) alentemol; apomorphine; biperiden; bromocriptine; cabergoline; carmoxirole; ciladopa; dopexamine; fenoldopam; ibopamine; levodopa; lisuride; methylenedioxypropylnoraporphine; naxagolide; *N*-allylnoraporphine; pergolide; pramipexole; propylnorapomorphine; protokylol; quinagolide; quinpirole; ropinirole; roxindole; talipexole; terguride; trihexyphenidyl; and trihydroxyaporphine and salts and combinations thereof;

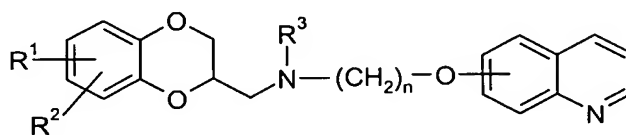
(b) a compound of Formula (0.0.1):



(0.0.1)

wherein R is -H, -OH, (C₁-C₄) alkylcarbonyloxy-, (C₁-C₄) alkylthio-, or -NR^aR^b where R^a and R^b are independently -H, -CH₃, -CH₂CH₃, or *n*-propyl; and R¹ and R² are independently -CH₃, -CH₂CH₃, *n*-propyl, or allyl; or a pharmaceutically acceptable salt thereof;

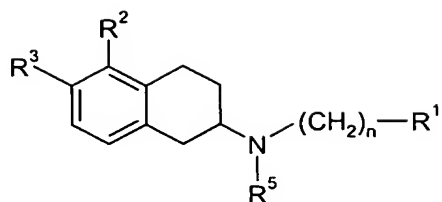
(c) a compound of Formula (0.0.2):



(0.0.2)

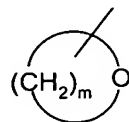
wherein *n* is 2-4; R¹ and R² are independently -H, -(C₁-C₆) alkyl, -(C₁-C₆) alkoxy, -(C₇-C₁₂) arylalkoxy, -(C₂-C₆) alkanoyloxy, -OH, halo, -NH₂, mono- or di-(C₁-C₆) alkylamino; -(C₂-C₆) alkanamido; or sulfonamido; R³ is -H, or -(C₁-C₆) alkyl; or R¹R² together are methylenedioxy, ethylenedioxy, or propylenedioxy; or a pharmaceutically acceptable salt thereof;

(d) a compound of Formula (0.0.3):



(0.0.3)

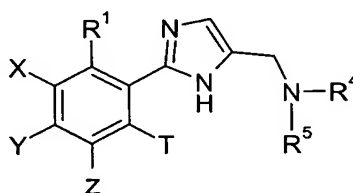
wherein R^2 is OA; and R^3 is $-H$ or OA; where A is $-H$, a hydrocarbyl radical of 1 to 3 carbon atoms, $-C(=O)R^4$, $-C(=O)NHR^4$, $-C(=O)N(R^4)_2$, or $-C(=O)OR^4$; provided that when R^2 and R^3 are OA, then R^2 and R^3 may be bonded together to form $-O-CH_2-O-$, or $-O-C(=O)-O-$; R^4 is (C_1-C_6) alkyl or an aromatic residue of 1-20 carbon atoms; n is 1-4; R^5 is unbranched (C_1-C_3) alkyl, or cyclopropylmethyl; and R^1 is (C_1-C_3) alkoxy, (C_3-C_6) cycloalkoxy, or a cyclic ether of partial Formula (0.1.1):



(0.1.1)

where m is 3 to 5; provided that when R^1 is (C_1-C_3) alkoxy, then R^3 cannot be $-H$; or a pharmaceutically acceptable salt thereof;

(e) a compound of Formula (0.0.4):

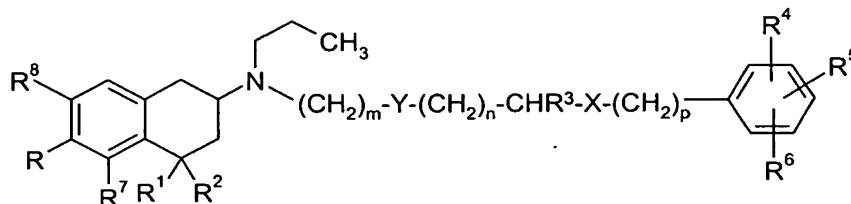


(0.0.4)

wherein R^1 and T are $-H$; halo; $-OH$; straight or branched (C_1-C_6) alkyl; or straight or branched (C_1-C_6) alkoxy; X and Z have the same meaning as R^1 and T additionally including SO_2R^6 where R^6 is straight or branched (C_1-C_6) alkyl; Y is $-H$; halo; $-NH_2$; or straight or branched (C_1-C_6) alkyl; R^4 and R^5 are $-H$; straight or branched (C_1-C_6) alkyl; phenyl (C_1-C_6) alkyl; or pyridyl (C_1-C_6) alkyl; and $-NR^4R^5$ is 2-(1,2,3,4-tetrahydroisoquinoliny) substituted by 0 to 2 of halo; $-OH$; straight or branched

(C₁-C₆) alkyl; or straight or branched (C₁-C₆) alkoxy; or a pharmaceutically acceptable salt thereof;

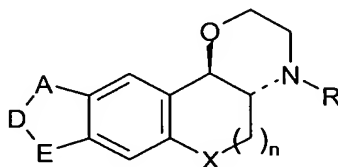
(f) a compound of Formula (0.0.5):



(0.0.5)

wherein m is 4 to 8; R, R⁷, and R⁸ are H or OH, provided at least one is H but not all three are H and provided R⁷ and R⁸ are not both OH, or one of R⁷ and R⁸ is H and the other is NHCHO, NHCH₃, NHSO₂CH₃, CH₂OH, or CH₃; R¹ and R² are H, (C₁-C₃) alkyl, or together form a cyclopropyl group with the carbon atom to which they are attached; n is 0 to 4; p is 0 or 1; R³ is H or (C₁-C₄) alkyl; Y is S, O, NHCO, CONH, or NH; X is NH, O, S, SO, SO₂, CO, or a single bond; and R⁴, R⁵, and R⁶ are H, OH, halo, (C₁-C₄) alkyl, (C₁-C₄) alkoxy, nitro, (C₁-C₄) alkylthio, amino, mono- or di-(C₁-C₄) alkylamino, (C₁-C₄) alkylsulfonyl, (C₁-C₄) alkoxycarbonyl, (C₁-C₄) alkylcarbonylamino, (C₁-C₄) alkylsulfonylamino, COOH, CONH₂, CH₂OH, or phenyl; or a pharmaceutically acceptable salt thereof;

(g) a compound of Formula (0.0.6):

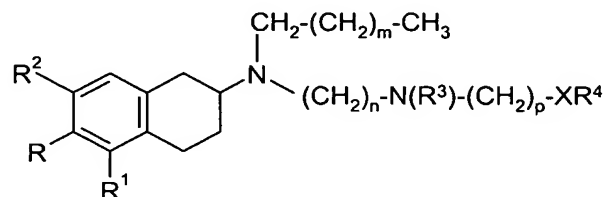


(0.0.6)

wherein A-D-E is CO(CH₂)_p; CH(OH)(CH₂)_p; S(O)_m(CH₂)₂; or S(O)_mCH=CH; where p is 2 or 3, and m is 0, 1, or 2; X is CH₂, or O when A-D-E does not contain S; n is 0 or 1 when X is CH₂, or n is 1 when X is O; and R is H, (C₁-C₁₀) alkyl, (C₃-C₁₀) alkenyl, or (C₃-C₁₀) alkynyl each optionally substituted by (C₃-C₈) cycloalkyl,

phenyl, thienyl, or pyridyl, each optionally substituted by 1 to 3 of halo, OH, (C₁-C₆) alkyl, or (C₁-C₆) alkoxy; or a pharmaceutically acceptable salt thereof;

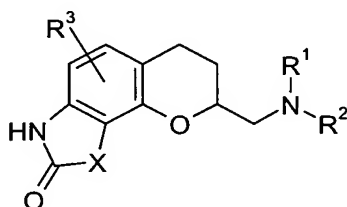
(h) a compound of Formula (0.0.8):



(0.0.8)

wherein R, R¹, and R² are H, or OH, provided at least one, but not all three thereof is hydrogen and provided R¹ and R² are not both OH; R³ is H or (C₁-C₄) alkyl; R⁴ is phenyl, thienyl, imidazolyl, pyridyl, or isoxazolyl, each optionally substituted by halo, (C₁-C₃) alkyl, or (C₁-C₃) alkoxy; X is CH₂; NH; S; SO; SO₂; CO; CF₂; or O; or a direct bond when R⁴ is one of the above-recited 5- or 6-membered heterocyclyl residues; m is 1 or 2; and n is 3 to 8; or a pharmaceutically acceptable salt thereof;

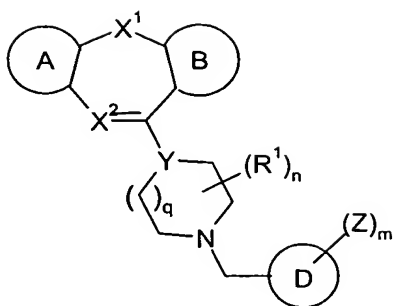
(i) a compound of Formula (0.0.9):



(0.0.9)

wherein X is (CH₂)_n where n is 1 to 3; R¹ is -H; (C₁-C₆) alkyl; hydroxy(C₁-C₆) alkyl; cyclo(C₃-C₇) alkylmethyl; bicyclo(C₇-C₉) alkylmethyl; or - (CH₂)_m-Y-Ar where m is 0 to 4, Y is CH₂ and Ar is phenyl; halophenyl; (C₁-C₆) alkylphenyl; di-(C₁-C₆) alkylphenyl; or (C₁-C₆) alkoxyphenyl; R² is H or (C₁-C₆) alkyl; and R³ is H; halo; (C₁-C₆) alkyl; (C₁-C₆) alkoxy; or hydroxy; or a pharmaceutically acceptable salt thereof;

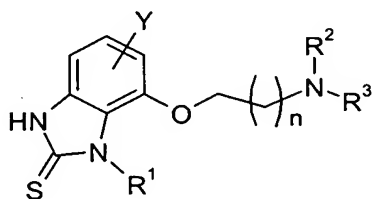
(j) a compound of Formula (0.0.10):



(0.0.10)

wherein A and B are benzene unsubstituted or substituted with 1 to 3 of OH, halo, (C₁-C₄) alkyl, NH₂, NO₂, CN, halo substituted (C₁-C₄) alkyl, halo substituted (C₁-C₄) alkoxy, (C₁-C₄) alkoxycarbonyl, cyclo(C₃-C₇) alkyl, (C₁-C₄) alkylthio, tetrazolyl, N-piperidinyl, N-piperazinyl, N-morpholinyl, acetamido, (C₁-C₄) alkylsulfonyl, sulfonamido, or OSO₃H; X¹ is O, NH, N-(C₁-C₄) alkyl, or N-acetyl; X² is N=; Y is CH or N; Z is cyano; R¹ is (C₁-C₄) alkyl; m is 1 to 3; n is 0 to 2; q is 1 or 2; and D is benzene; or a pharmaceutically acceptable salt thereof;

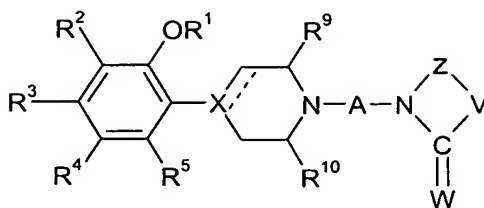
(k) a compound of Formula (0.0.12):



(0.0.12)

wherein R¹ is -H, or (C₁-C₆) alkyl; R² is -H, or (C₁-C₆) alkyl; R³ is -H, straight or branched (C₁-C₁₀) alkyl, cyclohexylmethyl, or -(CH₂)_mAr where m is 1 to 5, and Ar is phenyl, naphthyl, thienyl, furanyl, or pyridinyl, each substituted by 0 to 2 substituents independently selected from (C₁-C₆) alkyl, halo, (C₁-C₆) alkoxy, trifluoromethyl, and 4-fluorobutyrophenone; -NR²R³ is 1,2,3,4-tetrahydroquinolin-1-yl or 1,2,3,4-tetrahydroisoquinolin-2-yl; n is 1 or 2; and Y is halo, (C₁-C₆) alkyl, or (C₁-C₆) alkoxy; or a pharmaceutically acceptable salt thereof;

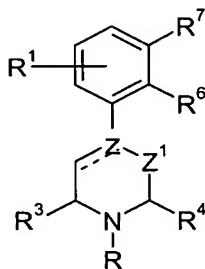
(l) a compound of Formula (0.0.13):



(0.0.13)

wherein A is (C₁-C₃) alkylene, or cyclo(C₃-C₇) alkylene; R¹ is (C₃-C₁₀) alkyl, cyclo(C₃-C₇) alkyl, cyclo(C₃-C₇) alkyl-(C₁-C₄) alkyl, trifluoromethylsulfonyl, or (C₁-C₄) alkylsulfonyl; R² to R⁵ are H, halo, (C₁-C₄) alkyl, (C₁-C₄) alkoxy, (C₁-C₄) alkylthio, OH, (C₁-C₄) alkylsulfonyl, (C₁-C₄) alkylcarbonyl, CN, phenylcarbonyl, CF₃, cyclo(C₃-C₇) alkyl, cyclo(C₃-C₇) alkyl-(C₁-C₄) alkyl, NO₂, mono- or di-(C₁-C₄) alkylamino; R⁹ and R¹⁰ are H, (C₁-C₄) alkyl, or together form an ethylene or propylene bridge; W is O or S; V is O, S, CR⁶R⁷, or NR⁸ where R⁶, R⁷, and R⁸ are H, (C₁-C₄) alkyl, cyclo(C₃-C₇) alkyl, (C₁-C₄) alkyl-phenyl, or phenyl, or R⁶ and R⁷ together constitute a 3-7 membered spiro-joined ring; Z is -(CH₂)_m- where m is 2 or 3, or Z is -CH=CH-; and the dashed line represents an optional bond such that when present, X is C, and when absent, X is N or CH; or a pharmaceutically acceptable salt thereof;

(m) a compound of Formula (0.0.14):

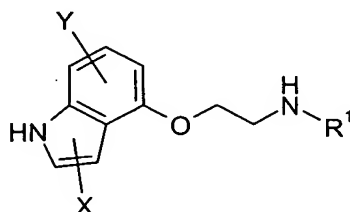


(0.0.14)

wherein R is -CH₂Z²R⁵; R¹ is -H or -F; R³ and R⁴ are independently -H, or (C₁-C₄) alkyl; R⁵ is phenyl, furyl, or thienyl each substituted by 0 to 3 of -OH, halo, (C₁-C₄) alkoxy, (C₁-C₄) alkyl, -CN, -C(=O)NH₂, or mono- or di-(C₁-C₄) alkylaminocarbonyl; R⁶ and R⁷ are independently atoms that are necessary to complete a heterocyclic ring that is substituted by 0 to 2 of (C₁-C₄) alkyl, (C₁-C₄) alkoxy, or oxo; Z is -C- or -N-; Z¹ is -CH₂- or -CH₂CH₂-; Z² is 1,3-phenylene substituted by 0

to 3 of -OH , halo, $(\text{C}_1\text{-C}_4)$ alkoxy, or $(\text{C}_1\text{-C}_4)$ alkyl; the dashed line is a bond when Z is C and is absent when Z is N; or a pharmaceutically acceptable salt thereof;

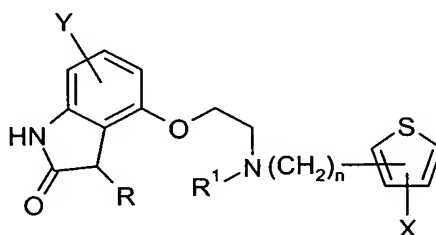
(n) a compound of Formula (0.0.16):



(0.0.16)

wherein R^1 is $(\text{C}_1\text{-C}_{10})$ alkyl, cyclo $(\text{C}_3\text{-C}_7)$ alkyl, $(\text{C}_1\text{-C}_4)$ alkyl, phenyl $(\text{C}_1\text{-C}_4)$ alkyl, thienylmethyl, furanylmethyl, pyridinylmethyl, 4-fluorobutyrophenone, or 6-fluoro-1,2-benzisoxazolylpropyl; X is H, halo, CN, $(\text{C}_1\text{-C}_6)$ alkyl, acetyl, trifluoroacetyl, CF_3 , or formyl; and Y is H, halo, $(\text{C}_1\text{-C}_6)$ alkoxy, or $(\text{C}_1\text{-C}_6)$ alkyl; or a pharmaceutically acceptable salt thereof;

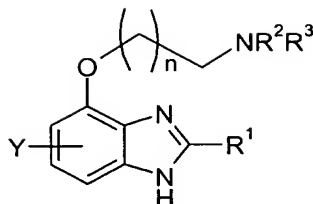
(o) a compound of Formula (0.0.18):



(0.0.18)

wherein Y is -H , halo, or $\text{-(C}_1\text{-C}_4\text{) alkoxy}$; R is -H , or $\text{-(C}_1\text{-C}_4\text{) alkylthio}$; R^1 is -H , or $\text{-(C}_1\text{-C}_4\text{) alkyl}$; X is -H , halo, $\text{-(C}_1\text{-C}_4\text{) alkyl}$, $\text{-(C}_1\text{-C}_4\text{) alkoxy}$, or phenyl; and n is 1-4; or a pharmaceutically acceptable salt thereof;

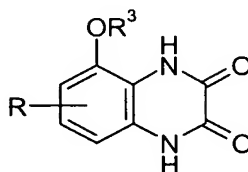
(p) a compound of Formula (0.0.19):



(0.0.19)

wherein R^1 is H, CF_3 , C_2F_5 , C_3F_7 , (C_1-C_6) alkyl, or benzyl optionally substituted by 1 to 3 of halo, NH_2 , NO_2 , OH , or (C_1-C_6) alkoxy; R^2 is H or (C_1-C_6) alkyl; R^3 is H, (C_1-C_{10}) alkyl, cyclohexylmethyl, or $(CH_2)_mAr$ where Ar is phenyl, thienyl, furanyl, or pyridinyl optionally substituted by 1 or 2 of halo, (C_1-C_6) alkoxy, CF_3 , or (C_1-C_6) alkyl; NR^2R^3 is 1,2,3,4-tetrahydroquinolin-1-yl, or 1,2,3,4-tetrahydroisoquinolin-2-yl; Y is halo, (C_1-C_6) alkyl, NH_2 , or (C_1-C_6) alkoxy; and n is 1 to 5; or a pharmaceutically acceptable salt thereof;

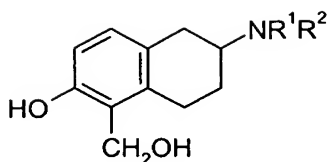
(q) a compound of Formula (0.0.20):



(0.0.20)

wherein R is halo, $-(C_1-C_4)$ alkyl, or $-(C_1-C_3)$ alkoxy; and R^3 is $-(CH_2)_nNR^1R^2$ where n is 1-2, and R^1 and R^2 are independently -H, $-(C_1-C_6)$ alkyl, or aryl $-(C_1-C_4)$ alkyl- where aryl is phenyl, naphthyl, or thienyl, or NR^1R^2 is 1,2,3,4-tetrahydroquinolin-1-yl, or 1,2,3,4-tetrahydroisoquinolin-2-yl; or a pharmaceutically acceptable salt thereof;

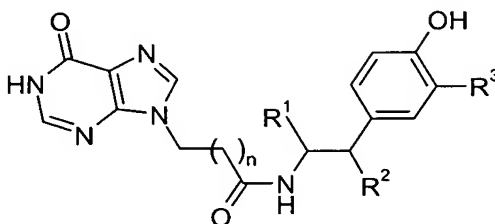
(r) a compound of Formula (0.0.21):



(0.0.21)

wherein R¹ and R² are independently -H, or -(C₁-C₄) alkyl; or a pharmaceutically acceptable salt thereof;

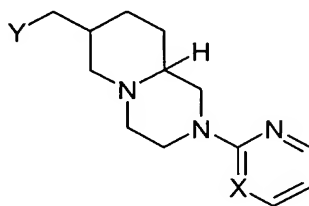
(s) a compound of Formula (0.0.22):



(0.0.22)

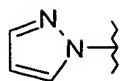
wherein R¹ is H or C(=O)OR⁴; R² and R³ are H or OH; R⁴ is H, NH₂, (C₁-C₄) alkyl, or (C₁-C₄) alkylamino; and n is 0 to 5; or a pharmaceutically acceptable salt thereof;

(t) a compound of Formula (0.0.23):

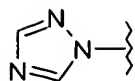


(0.0.23)

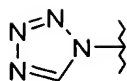
wherein X is N or CH; and Y is a moiety of partial Formulas (0.1.2) through (0.1.5):



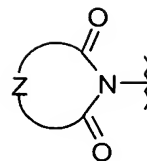
(0.1.2)



(0.1.3)

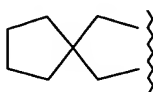


(0.1.4)

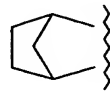


(0.1.5)

where Z is a moiety of partial Formulas (0.1.6) or (0.1.7):



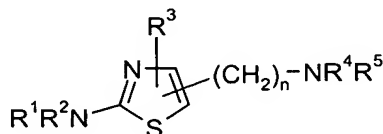
(0.1.6)



(0.1.7)

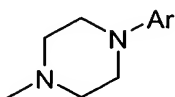
or Z is $-\text{SCH}_2-$, $-\text{OCH}_2-$, or $-\text{Y}^1(\text{CH}_2)_n-$, where n is 1 to 2, and Y^1 is $-\text{CH}_2-$, $-\text{NH}-$; or $-\text{N}(\text{CH}_3)-$; or a pharmaceutically acceptable salt thereof;

(u) a compound of Formula (0.0.24):

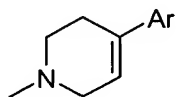


(0.0.24)

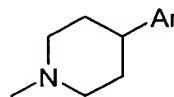
wherein n is 2 to 6; R^1 and R^2 are $-\text{H}$, (C_1-C_4) alkyl, phenyl, or (C_1-C_4) alkanoyl; R^3 is (C_1-C_4) alkyl, thienyl, or phenyl optionally substituted by halo, (C_1-C_4) alkyl, or (C_1-C_4) alkoxy; and NR^4R^5 is $-\text{NR}^6(\text{CH}_2\text{CH}_2\text{R}^7)$ where R^6 is $-\text{H}$ or $-(\text{C}_1-\text{C}_4)$ alkyl and R^7 is thienyl or phenyl optionally substituted by halo, (C_1-C_4) alkyl, or (C_1-C_4) alkoxy; or NR^4R^5 is Q^1 , Q^2 , or Q^3 , which are moieties of partial Formulas (0.1.8) through (0.1.10), respectively:



(0.1.8)



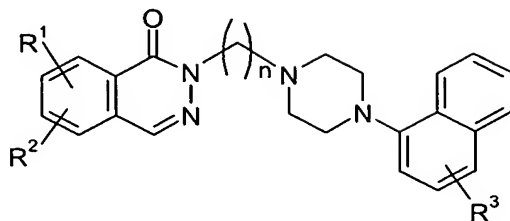
(0.1.9)



(0.1.10)

where Ar is pyridyl, pyrimidinyl, thienyl, or phenyl; or a pharmaceutically acceptable salt thereof;

(v) a compound of Formula (0.0.25):

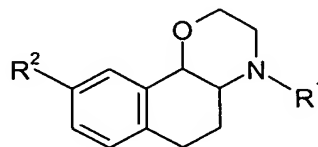


(0.0.25)

wherein R^1 and R^2 are H, (C₁-C₄) alkyl, halo, NO₂, NH₂, (C₁-C₄) alkanoylamino, or (C₁-C₄) alkoxy; n is 2 to 5; and R^3 is H, OCH₃, or F; or a pharmaceutically acceptable salt thereof;

— and —

(w) a compound of Formula (0.0.26):



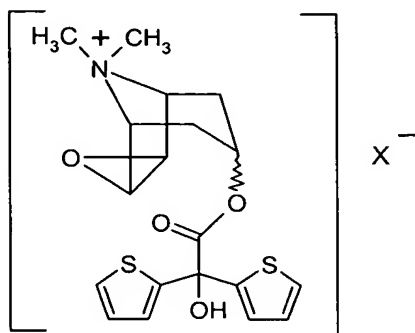
(0.0.26)

wherein R^1 is -(C₁-C₆) alkyl or -(C₃-C₆) alkenyl substituted by 0 to 2 of -(C₃-C₇) cycloalkyl, phenyl, thienyl, or pyridyl, each substituted in turn by 0 to 2 of halo, -OH, -(C₁-C₄) alkyl, or -(C₁-C₄) alkoxy; and R^2 is -CN, -C(=O)CH₃, -C(=O)NR³R⁴, or -C(=O)R³, where R^3 and R^4 are -H, or -(C₁-C₄) alkyl; or a pharmaceutically acceptable salt thereof.

24. The composition according to Claim 22 wherein the dopamine D₂-receptor agonist is a member selected from the group consisting of alentemol hydrobromide; apomorphine hydrochloride; bromocriptine mesylate; cabergoline; fenoldopam mesylate; levodopa; lisuride; naxagolide hydrochloride; pergolide mesylate; pramipexole dihydrochloride; quinpirole hydrochloride; ropinirole hydrochloride; and talipexole.

25. The composition according to Claim 24 wherein the dopamine D2-receptor agonist is selected from the group consisting of bromocriptine mesylate, naxagolide hydrochloride, cabergoline, pergolide mesylate, quinpirole hydrochloride, and ropinirole hydrochloride.

26. The composition according to Claim 20 wherein the anti-cholinergic agent comprises a compound of Formula (1.1.1):



(1.1.1)

wherein X⁻ is a physiologically acceptable anion.

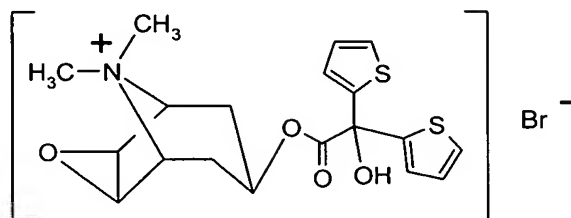
27. The composition according to Claim 26 wherein the physiologically acceptable anion, X⁻, is a member selected from the group consisting of fluoride, F⁻; chloride, Cl⁻; bromide, Br⁻; iodide, I⁻; methanesulfonate, CH₃S(=O)₂O⁻; ethanesulfonate, CH₃CH₂S(=O)₂O⁻; methylsulfate, CH₃OS(=O)₂O⁻; benzene sulfonate, C₆H₅S(=O)₂O⁻; *p*-toluenesulfonate, and 4-CH₃-C₆H₅S(=O)₂O⁻.

28. The composition according to Claim 27 wherein the physiologically acceptable anion, X⁻, is bromide, Br⁻.

29. The composition according to Claim 29 wherein the anti-cholinergic agent comprises a 3- α compound.

30. The composition according to Claim 29 wherein the anti-cholinergic agent comprises tiotropium bromide, (1 α , 2 β , 4 β , 5 α , 7 β)-7-[(hydroxydi-2-thienylacetyl)oxy]-

9,9-dimethyl-3-oxa--9-azoniatricyclo[3.3.1.0^{2,4}] non-ane bromide, represented by Formula (1.1.2):

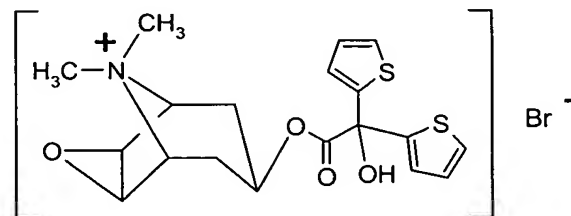


(1.1.2)

31. A package comprising a device containing the composition according to claim 20 for simultaneous or sequential delivery of components (I) and (II) in the form of an aerosol or dry powder.

32. The package according to Claim 31 wherein the composition comprises a dopamine D2-receptor agonist selected from the group consisting of bromocriptine mesylate, naxagolide hydrochloride, cabergoline, pergolide mesylate, quinpirole hydrochloride, and ropinirole hydrochloride:

33. The package according to Claim 31 wherein the composition comprises tiotropium bromide, (1 α , 2 β , 4 β , 5 α , 7 β)-7-[(hydroxydi-2-thienylacetyl)oxy]-9,9-dimethyl-3-oxa--9-azoniatricyclo[3.3.1.0^{2,4}] non-ane bromide, represented by Formula (1.1.2):



(1.1.2)

34. The package according to Claim 33 wherein the device is a metered dose inhaler, or a dry powder inhaler.